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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,373	05/16/2001	Robert P. Kimberly	UAB-14202/22	5348

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EXAMINER
SAKELARIS, SALLY A

ART UNIT	PAPER NUMBER
1634	16

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,373	KIMBERLY, ROBERT P.	
	Examiner	Art Unit	
	Sally A Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 26-35* is/are pending in the application.

4a) Of the above claim(s) *22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 26-35* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-21 and 26-35, drawn to methods of determining susceptibility in paper No. 15, filed 10-10-2002 is acknowledged.

Specification

The information disclosure statement filed October 1, 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It should be noted that the information referred to therein has not been considered by the examiner.

Priority

Acknowledgement of the provisional application drawn to this same subject matter has been made. The filing date of the instant claims is deemed to be the filing date of the provisional application 60/094096, 07/23/1998.

Claim Objections

Claim 35 is objected to because of the following: Claim 35 is a product claim and depends from method claims, i.e., claim 35 does not properly depend from claims "1 or 22" since a claim to a product cannot depend from a claim to a method of using a product (SEE MPEP 608.01(n)). The improper dependency is objected to and appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claims 31-33 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Chee et al.(US Patent 5,856,104)

Chee et al. teach a commercial package and/or a reagent kit, comprising reagents for the PCR based detection of polymorphisms and further teach the accompaniment of "instructions for carrying out the methods."(Col. 13)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-21 and 26-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of the invention. Claims 1-21 and 26-35 are broadly drawn to methods of correlating the ability of a cell to bind IgA and cellular susceptibility to a disease. The specification does not at all enable correlating the ability of any cell to bind IgA, to cellular susceptibility to any disease. The specification does not specify any examples of such well-established, *in–vitro* model systems or evidence for the ability of a cell's receptors(FcαRI)to bind IgA and its predictable association with cellular susceptibility to any disease. The examples that are taught in the specification include only SNPs in the coding regions of FcγRIIA, FcγRIIIA, and FcγRIIIB and a belief that a "precedent" is established by these findings, that these SNPs influence the risk for Periodontal Disease(PD). The specification continues on to conclude that the findings for one gene coding for the IgG receptor can be applicable to that of another gene coding for the different, IgA receptor. The specification teaches that the "knowledge that PD lesions are rich in both IgG and IgA."(Pg 23, line 20-23) is enough to lead one skilled in the art to believe that their receptors function exactly the same. The specification merely prophesizes

that as a result of these previous findings with the IgG receptor, "the present invention identifies novel SNPs in FcαRI." It is highly unpredictable to extrapolate findings from the Fcγ molecules to the entirely different molecules defined by FcαRI. In addition, it is important to note that even if applicant would enable the detection of SNPs in the FcαRI gene, only those genotypes taught in the specification on Pg. 33 in example 3, would be enabled, not all genotypes of the receptor. Furthermore, this method includes i). identifying a FcαRI genotype, ii). quantifying IgA binding by a cell with said genotype, and iii). comparing IgA binding by said cell and IgA binding by a second cell, said second cell expressing a second FcαRI genotype. Furthermore, while the method's step i), of identifying a genotype would include the "how to make" portion of the enablement requirement, it still omits the "how to use portion" as the specification omits any teaching of how to use the discovered genotype once it has been discovered. With respect to step ii), it is unclear how the amount of bound IgA relates to the genotype of a cell. The specification does not teach the effect that the amount of bound IgA has on the genotype of the cell or vice versa. Lastly, as in steps i) and ii), the specification does not teach which genotype said first cell has nor what genotype said second cell has and why either of these would be significant as related to each cell's ability to bind IgA.

With respect to claim 34, although directed to a product, the reagents will be used to identify individual susceptibility to a disease, a feat that as previously mentioned lacks enablement because of the great unpredictability that exists in such a research project. The nature of this invention is quite unpredictable because it requires a reliance on the prophetic testimony by applicant that the progression of any disease will in fact be evident through the detection of any FcαRI genotype.

Scope of the invention. The scope of the invention is very broad, claiming methods for correlating the ability of any type of cell to bind IgA and the cellular susceptibility to any disease. Much unpredictability exists in the broad claiming of any type of cell and having, as in steps i) ii) and iii)'s, any genotype being correlated to any amount of bound IgA by the cell expressing said genotype. Furthermore, as alluded to in the Nature of the invention, even if applicants would enable detection of SNPs in the FcαRI gene, their scope would still be limited to those delineated in example 3 of the specification.

State of the art. The prior art does not disclose a method for correlating the ability of a cell to bind IgA and cellular susceptibility to a disease, thus the invention appears to be novel in terms of the prior art. However, the lack of support from the prior art for the ability of a genotype of the FcαRI, IgA receptor, to have such far-reaching effects such as into the manifestation of any disease, results in the invention being unpredictable in terms of its use as presently claimed. Furthermore, as the present application relies on the extrapolation from data involving the receptor for the IgG molecule to define characteristics for the receptor of the IgA molecule, the art teaches great unpredictability associated with this practice. The specification's reliance on the IgG receptor data implies that IgG and IgA are identical. However, Morton et al. teach "the cDNA encoding the myeloid FcαR has been characterized and was found to encode a 30-kDa peptide with two extracellular Ig-like domains" the reference goes on to teach though that, "the gene structure indicates FcαR to represent a more distantly related member of the immunoglobulin receptor gene family." (JBC, 1995) Furthermore, Carayannopoulos et al. teach while the FcαR receptor "shows similarity to the high affinity FcεR and the three FcγR but is more distantly related to these receptors than they are to one another."(J. Exp. Med. 1996) In

addition to the prior art, the post date art also teaches variation between these two receptor types. Wines et al teach that the "comparison of the FcγRI:IgA interaction showed considerable differences from the well-defined FcγR:IgG and FcεRI:IgE interactions. Unlike other Fc receptors, in FcαRI the ligand binding site appears to be in the first domain, not the second, and in IgA, unlike IgG or IgE, the receptor binding site is located at the interface between CH2 and CH3, not the lower hinge of CH2 as for IgG or its equivalent area in IgE Cε2."(AAI, 2001) Such variance between IgG receptors and those for IgA makes drawing conclusions and the subsequent extrapolations about the two molecules, highly unpredictable.

Number of working examples and Guidance provided by applicant. The instant specification only provides guidance and working examples concerning the FcγRI, RIIA, RIIIA, and RIIIB IgG receptor molecules. Considering the unpredictability surrounding the extrapolation of data from experiments using different receptor molecules, as pointed out in the Nature of the invention section of this rejection, the skilled artisan would have to practice undue and unpredictable trial and error experimentation in order to practice the invention with the genotypes of IgA receptors(FcαRI) that are not the genotypes of IgG receptors(FcγRI..etc.). In addition, considering the lack of working examples showing the association between a particular SNP and a specific disease, even more unpredictability exists.

Level of skill in the art. The level of skill involved in relating characteristics of such different molecules(FcαRI and FcγRI etc) to each other is very high if not impossible. Additionally, the functional use of such assumed similar properties from such different molecules is seen, in this instance, to be prophetic.

Unpredictability of the art. There are examples of differences in the IgG receptor and that being claimed, the IgA as illustrated in the State of the Art section. Both the prior art and the instant specification are deficient in terms of teaching the applicability of IgG receptor data to that of IgA genotype effects. Furthermore, the lack of teachings of how to use any genotype of the FcαRI gene, and also how the amount of IgA binding relates to this genotype both contribute to the great unpredictability involved in making and using this invention. In light of these deficiencies, the skilled artisan would be forced to practice undue and unpredictable trial and error experimentation when practicing the instant invention.

Considering the Nature of the invention, the guidance provided by both the prior art and the instant specification, and the broad scope of the invention, it is clear that the skilled artisan would be required to practice undue and unpredictable trial and error experimentation to practice the invention that is claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12 and 26-33 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-12 and 35 are indefinite for failing to recite a final process step that relates back with the preamble. Claim 1 is drawn to a method for correlating the ability of a cell to bind IgA and cellular susceptibility to a disease. However, the final process step is one of comparing IgA binding by said cell and IgA binding by a second cell, said second cell expressing a second

FcαRI genotype. Accordingly, it is unclear as to whether the claim is intended to be limited to methods for correlating the ability of a cell to bind IgA and cellular susceptibility to a disease, referred to in the preamble, or just to comparing IgA binding by said cell and IgA binding by a second cell, said second cell expressing a second FcαRI genotype. Applicant should amend this claim to clarify.

B. Claims 26-30 are indefinite for failing to recite a final process step that relates back with the preamble. Claim 26 is drawn to a method of prognosticating a human immunoresponse to a disease. However, the final process step is one of determining clinical outcome for said patient based on said patient genotype. Accordingly, it is unclear as to whether the claim is intended to be limited to methods of prognosticating a human immunoresponse to a disease or to determining clinical outcome for said patient based on said patient genotype. Applicant should amend this claim to clarify.

C. Claims 31-33 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 31-33 provide for the use of a SNP in the FcαRI genotype to identify individual susceptibility to a disease, but, since the claim does not set forth any steps involved in the method, it is unclear what method the applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

D. Claims 13-21 and 35 are indefinite as the claims do not clarify the relationship between genotyping DNA and determining FcαRI alleles. For example, determining the genotype of an individual doesn't necessarily lead one to the FcαRI alleles specific to an individual, it merely

provides you with the genotype of that individual. The claims should be amended to identify the relationship being claimed.

E. Claim 35 is indefinite as it is improper for a claim to refer generically to examples set forth in the specification and it is unclear as to what would be considered a method "substantially as described herein in any of the examples." Rather, "substantially" has not been defined in the specification and it is unclear as to how the method can be modified from the methods disclosed in the specification. Additionally, it is unclear as to what reagents are intended to be included in the kit since the kit only recites an intended use, but does not set forth any specific reagents. Appropriate correction is required.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Friday from 7:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703)308-1152. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

12/30/2002

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER

Sally Sakelaris

Sally Sakelaris